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Keratinocytes as a target for gene therapy. Sustained production of erythropoietin in mice by human keratinocytes transduced with an adenoassociated virus vector.**Descamps V, Blumenfeld N, Beuzard Y, Perricaudet M.**

Department of Dermatology, Hopital Bichat, Paris, France.

BACKGROUND AND DESIGN: Keratinocytes are ideal targets for somatic gene therapy. Among the viral gene transfer systems, adenoassociated virus vectors have recently gained attention. We studied the feasibility of using adenoassociated virus-transduced human keratinocytes to provide a long-term, high-level production of a therapeutic factor after implantation in mice. **RESULTS:** Transduction of HeLa cells by an adenoassociated virus vector was ascertained by transfer of the beta-galactosidase reporter gene, which was visualized by the blue staining of infected cells after fixation and coloring by X-Gal (the substrate of the reaction for beta-galactosidase activity). In a second step, 2 HeLa cell lines transduced with an AAV harboring the erythropoietin complementary DNA and producing high amounts of erythropoietin in vitro were isolated. After implantation in nude mice, a high-level and long-term increase in hematocrit (for the 1-month duration of the study) was found, which was correlated to the size of the induced tumor. **CONCLUSIONS:** Adenoassociated virus-transduced HeLa keratinocytes provide high-level, stable, and long-term production of a therapeutic protein in mice. These results must now be extended to human primary keratinocytes.

PMID: 8859032 [PubMed - indexed for MEDLINE]

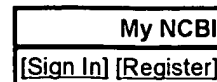
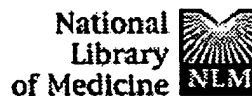
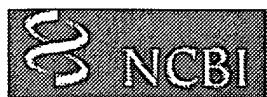
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L1	11	530/395.ccls. and EPO and lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/13 14:37
S1	122	530/395.ccls. and EPO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/09/07 07:24
S2	13	530/395.ccls. and EPO SAME CHO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/09/07 07:24
S3	1212	EPO SAME composition	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/12 00:06
S4	0	EPO SAME composition SAME glycosylated and "N-acetyl lactosamine" and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:12
S5	0	EPO SAME composition SAME glycosylated and "N-acetyl lactosamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:12
S6	40	EPO SAME composition SAME glycosylated	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:12
S7	1	EPO SAME composition SAME glycosylated and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:14
S8	1	EPO SAME composition SAME lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:15
S9	3	EPO SAME composition and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:17
S10	19	EPO and composition and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:17
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S12	0	EPO.ab. and composition and glycosylated and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:17
S13	0	EPO.ti. and composition and glycosylated and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:17
S14	8	erythropoietin and composition and glycosylated and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:18
S15	16	EPO and composition and glycosylated and lactosamine and carbohydrate	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:18
S16	93	EPO.ab. SAME composition.ab.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:19
S17	2	EPO.ab. and composition.ab. and glycosylated.ab.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:21
S18	1	EPO.ab. and EPO SAME composition SAME glycosylated	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:21
S19	125	EPO.ab. and EPO SAME composition	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:22
S20	0	EPO.ab. and EPO SAME composition and lactosamine SAME glycosylated	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:22
S21	2	EPO.ab. and EPO SAME composition and lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:22
S22	35	EPO.ab. and EPO SAME composition and glycosylat\$3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:23
S23	3	EPO.ab. and EPO SAME composition SAME glycosylat\$3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:23

S24	35	EPO.ab. and EPO SAME composition and glycosylat\$3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:23
S25	3	EPO.ti. and EPO SAME composition and glycosylat\$3	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/06/02 11:23
S26	2	"9635718".did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/08/13 00:33
S27	5	"267678".did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/08/13 00:37
S28	4	"9512684".did.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/08/13 00:55
S29	96	530/395.ccls. and EPO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/08/13 00:56
S30	0	530/395.ccls. and EPO and sialyated	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/08/13 00:59
S31	2	"5106954".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:19
S32	2	"6399333".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:19
S33	0	"6399333".pn. and glycosylation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:20
S34	0	"6399333".pn. and lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:20
S35	21	EPO and lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:22

S36	1	erythropoietin SAME lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:21
S37	0	"6399333".pn. and "high specific activity"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:22
S38	2	EPO SAME lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:22
S39	21	erythropoietin and lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/02 11:24
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S44	1285	EPO SAME composition	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 16:47
S45	9	EPO SAME composition SAME CHO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 17:04
S46	175	EPO SAME CHO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 17:04
S47	7	EPO.clm. and CHO.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 17:05

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S50	32	EPO SAME glycosylation SAME CHO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 17:17
S51	7	EPO SAME glycosylation SAME CHO and sialylation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 17:19
S52	2	"5459031".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/04 17:20
S53	2	"5459031".pn. and EPO	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/05 17:45
S54	1	"5459031".pn. and EPO and glucose	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/09/05 17:45
S55	432	EPO and N-acetyl	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:25
S56	4	EPO and N-acetyl ADJ lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:27
S57	4	EPO and "N-acetyl lactosamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:27
S58	2	EPO SAME "N-acetyl lactosamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:32
S59	2	EPO SAME "N-acetyl lactosamine" and "LacNac"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:33

S60	12	EPO and "N-acetyllactosamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:54
S61	3	EPO and "N-acetyllactosamine" and LacNac	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:42
S62	0	EPO and "N-acetyllactosamine". clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:47
S63	2	EPO and "N-acetyllactosamine".ab.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 14:47
S64	41	erythropoietin and "N-acetyllactosamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 15:04
S65	8	erythropoietin SAME "N-acetyllactosamine"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:08
S66	10	erythropoietin and LacNac	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 15:02
S67	8	erythropoietin and LacNac and N-glycan	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 15:02
S68	3	erythropoietin SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:26
S69	7	EPO SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:20
S70	1	EPO and tetraantennary SAME lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:20
S71	0	EPO and tetraantennary SAME N-actetylactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:20

S72	0	EPO and tetraantennary SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:20
S73	5	EPO and tetraantennary SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:22
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S76	2	erythropoietin SAME tetraantennary and N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:23
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S80	0	530/395.ccls. and erythropoietin and tetraantennary and N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/12 22:27
S81	0	EPO and enhance SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:28
S82	0	EPO and enhancing SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:28
S83	0	EPO and enhancing SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:28

S84	1	EPO and enhancing SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:28
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S86	3	EPO and increase SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:32
S87	3	erythropoietin and increase SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:31
S88	0	EPO and increasing SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:32
S89	1	EPO and increasing SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:32
S90	0	EPO and increasing SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:32
S91	2	EPO and increase SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:33
S92	2	erythropoietin and increase SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:33
S93	0	erythropoietin and increasing SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:33
S94	0	increasing SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:33
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S97	0	enhancing SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:37
S98	0	enhancing SAME N-acetyllactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:37
S99	2	enhancing SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:38
S10 0	1	increase SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:39
S10 1	1	increasing SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:40
S10 2	1	tetraantennary SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:40
S10 3	106	EPO SAME "human cell"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:46
S10 4	106	EPO SAME "human cells"	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:46
S10 5	0	EPO SAME "human cells" SAME tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:46
S10 6	0	EPO SAME "human cells" SAME N-acetyllactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:47
S10 7	1	EPO SAME "human cells" SAME N-acetyl-lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:48

S10 8	4	EPO SAME "human cells" SAME glycosylation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:49
S10 9	40	EPO SAME CHO SAME glycosylation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:49
S11 0	32	EPO SAME "CHO cells" SAME glycosylation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:49
S11 1	3	EPO SAME "CHO cells" SAME glycosylation SAME increasing	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:49
S11 2	4	EPO SAME "CHO cells" SAME glycosylation SAME increase	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:50
S11 3	238	EPO and increase SAME glycosylation	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:50
S11 4	10	EPO and increase SAME glycosylation and tetraantennary	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/04/17 09:50
S11 5	4	530/395.ccls. and EPO and lactosamine	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/04/13 14:37
S12 4	63	EPO SAME "HeLa"	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	ON	2005/04/12 00:06